FIGURE 1A

Amino acid sequence of human CCR5 [SEQ ID NO: 1]:

- 1 MDYQVSSPIY DINYYTSEPC QKINVKQIAA RLLPPLYSLV FIFGFVGNML VILILINCKR N-Terminus Transmembrane Domain l
- 61 LKSMTDIYLL NLAISDLFFL LTVPFWAHYA AAQWDFGNTM CQLLTGLYFI GFFSGIFFII LOOP 1 Transmembrane Domain 2 Loop 2 Transmembrane Domain 3
- 121 LLTIDRYLAV VHAVFALKAR TVTFGVVTSV ITWVVAVFAS LPGIIF**TRSQ KEGLHYTCSS**Loop 3 Transmembrane Domain 4 Loop 4
- 181 HFPYSQYQFW KNFQTLKIVI LGLVLPLLVM VICYSGILKT LLRCRNEKKR HRAVRLIFTI

 Transmembrane Domain 5 Loop 5
- 241 MIVYFLFWAP YNIVLLLNTF QEFFGLNNCS SSNRLDQAMQ VTETLGMTHC CINPILYAFV

 Transmembrane Domain 6 Loop 6 Transmembrane Domain 7
- 301 GEKFRNYLLV FFQKHIAKRF CKCCSIFQQE APERASSVYT RSTGEQEISV GL $\ensuremath{\textit{C-Terminus}}$

FIGURE 1B

Peptide fragments derived from human CCR5 that are used as target peptides:

N-terminal fragment [SEQ ID NO: 8]:

MDYQVSSPIYDINYYTSEPCQKINVKQIAARLLPPL

Loop 4 fragment [SEQ ID NO: 9]:

TRSQKEGLHYTCSSHFPYSQYQFWKNFQTLKI

Loop 6 fragment [SEQ ID NO: 3]:

EFFGLNNCSSSNRLDQAMQVTETLGMTHC

FIGURE 1C

A model of the secondary structure of human CCR5:

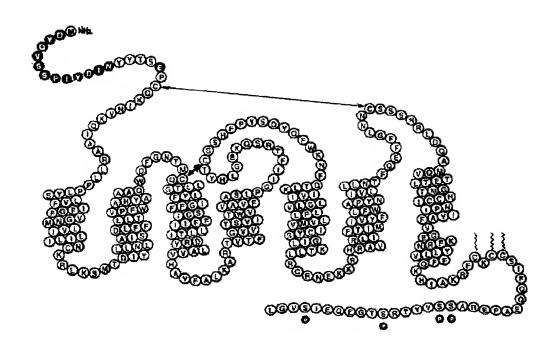
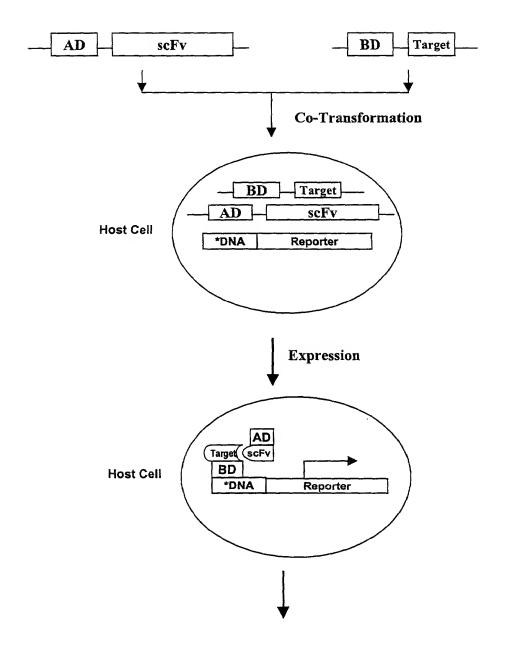
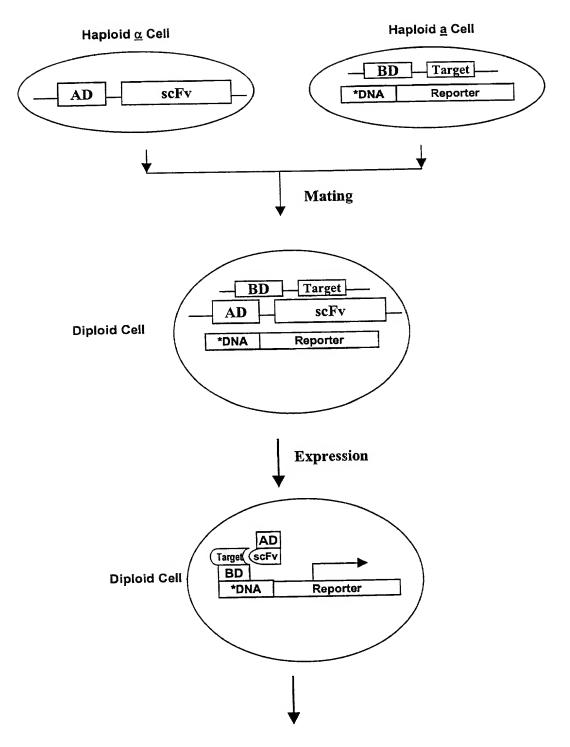


FIGURE 2A

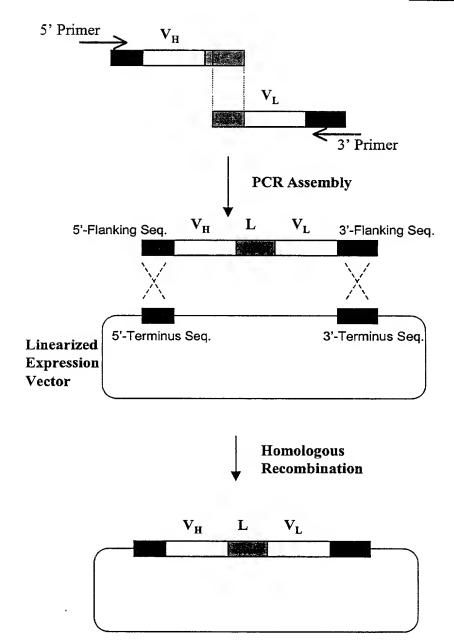


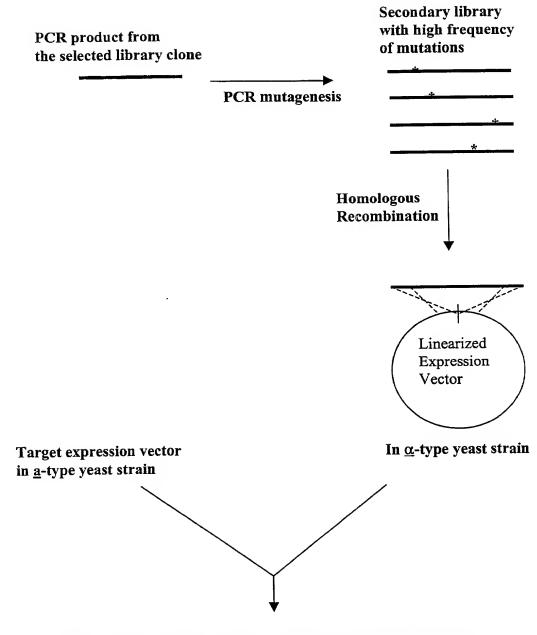
Selection of Clones Indicating Positive Binding Between the scFv antibody and the Target

FIGURE 2B



Selection of Clones Indicating Positive Binding Between the scFv antibody and the Target





Screening in yeast by mating and isolating high affinity clones

DNA sequence of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 16]:

CAGGTTACCTTGAAGGAGTCTGGTCCTACGTTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTGTCTGGGTT
CTCACTCAGCACTAGTGGAGTGAGTGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTTGAGTGGCTTGCAAGCATAA
ATTGGAATGATGATAAGTGCTACAGCCCATCTCTGAAAAGCAGGCTCACCATCACCAAGGACACCCCCAAAAACCAGGTG
GTCCTTGCAATGAGCAACATGGACCCTGCGGACACAGCCACATATTCCTGTGCACTCGATATGCCCCCCCATGATAGTGG
CCCGCAATCTTTTGATGCTTCTGATGTCTGGGGCCCAGGGACAATGGTCACCGTCTCTTCAGGCGGTGGTGGATCAGGCG
GCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTTCCTATGAGCTGATGCAGCTACCCTCAGTGTCCCGTGTCC
CCAGGACAGACAGCCAGCATCACCTGCTCTGGAGATAATTTTGGGGGATAAATATGCCTGCTGGTATCAACAGAAGCCAGG
CCGGTCCCCTGTGCTGGTCATTTATGGAGATAACAAGCGGCCCTCAGGGATCCCTGAGCGATTCTCTTGGCTCCAACTCTG
GGAACACAGCCACTCTGACCATCAGCGGGACCCAGGCTATGGATGAGGCTGACTATTACTGTCAGGCGTGGGACACCAGC
ACTGCTGTCTTCGGAACTGGGACCAAGCTCACCGTCCTA

Amino acid sequence of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 17]:

QVTLKESGPTLVKPTQTLTLTCTLSGFSLSTSGVSVGWIRQPPGKALEWLASINWNDDKCYSPSLKSRLTITKDTPKNQV

VLAMSNMDPADTATYSCALDMPPHDSGPQSFDASDVWGPGTMVTVSSGGGGSGGGGGGGGGGGGGGSYELMQLPSVSVS

PGQTASITCSGDNLGDKYACWYQQKPGRSPVLVIYGDNKRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCQAWDTS

TAVFGTGTKLTVL

0

DNA sequence of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 18]:

CAGGTGCAGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACTTGCACTGTCTCTGGTGC
CTCCATCGGTCATGACTACTGGAGCTGGATACGGCAGCCCCCAGGGGAGGACTGGAGTGGATTGGTTTCATCTTCTCG
ATGGGAGCACCAACTACAACCCCTCCCTCAACGGTCGAGLCACCATCTCACTCGACACGTCGAAGAATCAGCTCTCCCTG
AGGCTGACCTCTGTGACCGCTGCGGACACGGCCGTGTATTTCTGTGCGAGACACACGTCGAAGAATCAGCTCTCCCTG
AGGCTGACCTCTGTGACCGCTGCGGACACGGCCGTGTATTTCTGTGCGAGACTAAAGGGGGCGTGGTTATTGCTGAACC
CCCTTACTTCAGCTCCGACGGCATGGACGTCTGGGGCCAAGGGACCACCGTCACCGTCCCCTCAGGCGGTGGTCAGC
GCGGCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGAGGCAGCTCCGACATCTCAGCCCCCCTCAGCGTCTGGG
ACCCCCGGGCAGAGGGTCAGCATCTCTTGTTCTGGGAGCAGCTCCGACATCGGAAGTAATACTGTAAACTGGTACCAGCA
ACTCCCAGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCT
TCAAGTCTGGCACCTCAGCCTCCCTGGTCATCAGTGGCCTCCAGTCTGAGGATGAGGCTGATTATTATTGTGCAGCATGG
GATGAGAGCCTGAATGGTGTGTGTTCGGCGGAGGACCAAGG

Amino acid sequence of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 19]:

QVQLQESGPGLVKPSETLSLTCTVSGGSIGHDYWSWIRQPPGEGLEWIGFIFFDGSTNYNPSLNGRVTISLDTSKNQLSLRLTSVTAADTAVYFCARLKGAWLLSEPPYFSSDGMDVWGQGTTVTVPSGGGGSGGGGGGGGGGGGGGNFMLTQPPSASGTPGQRVSISCSGSSSDIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGFKSGTSASLVISGLQSEDEADYYCAAWDESLNGVVFGGGPR

FIGURE 5 (cont.)

DNA sequence of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 20]:

Amino acid sequence of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 21]:

QVQLQQWGAGLLKSWGTLSLTCAVSGASFSGYYWSWIRQPPGKGLEWIGEINHRGSTTYNPSLDGRVTISLDTSTNQISL
KLTSMTAADTAVYYCARTVAGTSDYWGQGTLVTVSSGSASAPTGGGGSGGGGGGGGGGGGGGGKTTLTQSPAFMSATPGD
KVSISCKASRDVDDDVNWYQQRPGEAPIFIIEDATTLVPGISPRFSGSGYGTDFTLTINNIDSEDAAYYFCLQHDNFPLT
FGGGTKVEIK

DNA sequence of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 22]:

CAGGTCACCTTGAAGGAGTCTGGTCCTACGCTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTCTCTGGGTT
CTCACTCAGAACTACTGGAGAGGGTGTGGGCTGGGTCCGTCAGCCCCCAGGAAAGGCCCTGGAATGGCTTGCACTCATTT
ATTGGGATGATGATAAGCGCTACAGCCCATCTCTGAAGAGCAGGCTCACCATCACCAAGGACACCTCCAAAAAAGCAGGTG
GTCCTTACAATGACCAACGTGGACCCAGCGGACACAGCCACCTATTACTGTACACACGAGCAATACTATTATGATACTAG
TGGTCAGCCATACTACTTTGACTTCTGGGGCCAGGGCACCCTGGTCACCGTCTCCTCAGGCGGTGGTGGATCAGGCGGC
GAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTAACATCCAGGTGACCCAGTCTCCATCCTCCCTGTCTGCATCT
GTAGGAGACAGAGTCACCATGACTTGCCGGGCGAGTCAGGACATTAGGAAGAATTTAAATTTGGTATCAGCAAAAACCAGG
GAAAGCCCCTAAGGTCCTGATCTACGATGCATCCGATTTGGAAACAGGGATCCCATCAAGGTTCAGTGGAAGTCTG
GGACAGATTTTATCCTCACCATCAGCAGCCTGCAGCCTGAAGATATTGCAACATACTACTGTCAACAGTCTGATTATTTA
CCGCTCACTTTCGGCGGAGGGACCAAAGTGGATATCAAA

Amino acid sequence of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 23]:

QVTLKESGPTLVKPTQTLTLTCTFSGFSLRTTGEGVGWVRQPPGKALEWLALIYWDDDKRYSPSLKSRLTITKDTSKKQV VLTMTNVDPADTATYYCTHEQYYYDTSGQPYYFDFWGQGTLVTVSSGGGGSGGGGGGGGGGGGGGGSNIQVTQSPSSLSAS VGDRVTMTCRASQDIRKNLNWYQQKPGKAPKVLIYDASDLETGIPSRFSGSGSGTDFILTISSLQPEDIATYYCQQSDYL PLTFGGGTKVDIK

DNA sequence of a variant of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEO ID NO: 24]:

Amino acid sequence of a variant of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 25]:

QVTLKESGPTLVKPTQTLTLTCTLSGFSLSTSGVSVGWIRQPPGKALEWLASINWNDDKCYSPSLKSRLTITKDTPKNQV VLAMSNMDPADTATYSCALDMPPHDSGPQSFDASDVWGPGTMVTVSSGGGGSGGGGGGGGGGGGGGSSYELMQLPSVSVS PGQTASITCSGDNLGDKYACWYQQKPGRSPVLVIYGDNKRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCQAWDTS TAVFGTGTKLTVL

DNA sequence of a variant of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 26]:

O

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACTTGCACTGTCTCTGGTGG
CTCCATCGGTCATGACTACTGGAGCTGGATACCGCAGCCCCCAGGGGAGGACTGGAGTGGATTGGTTTCATCTTCTCG
ATGGGAGCACCAACTACAACCCCTCCCTCAACGGTCGAGLCACCATCTCACTCGACACCGTCGAAGAATCAGCTCTCCTC
AGGCTGACCTCTGTGACCGCTGCGGACACGGCCGTGTATTTCTTGTGCGAGACTAAAGGGGGCGTGGTTATTGTCTGAACC
CCCTTACTTCAGCTCCGACGGCATGGACGTCTGGGGCCAAGGGACCACCGTCACCCTCTCAGGCGGTGGATCAG
GCGGCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGAGGCAGTAATTTTATGCTGACTCAGCCCCCCTCAGCGTCTGGG
ACCCCCGGGCAGAGGTCAGCATCTCTTGTTCTGGGAGCACATCGGAAGTAATACTGTAAACTGGTACCAGCA
ACTCCCAGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCT
TCAAGTCTGGCACCTCAGCCTCCCTGGTCATCAGTGGCCTCCAGTCTGAGGATGAGGCTGATTATTATTTTTGCAGCATCG
GATGAGAGCCTGAATGGTGTGTTCGGCGGAGGAACCAAGGTGACCGTCCTA

Amino acid sequence of a variant of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 27]:

FIGURE 6 (cont.)

DNA sequence of a variant of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 28]:

Amino acid sequence of a variant of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 29]:

Total Street

A STATE OF

QVQLQQWGAGLLKSWGTLSLTCAVSGASFSGYYWSWIRQPPGKGLEWIGEINHRGSTTYNPSLDGRVTISLDTSTNQISL KLTSMTAADTAVYYCARTVAGTSDYWGQGTLVTVSSGSASAPTGGGGSGGGGGGGGGGGGGGGGGETTLTQSPAFMSATPGD KVSISCKASRDVDDDVNWYQQRPGEAPIFIIEDATTLVPGISPRFSGSGYGTDFTLTINNIDSEDAAYYFCLQHDNFPLT FGGGTKVEIK

DNA sequence of a variant of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 30]:

CAGGTCACCTTGAAGGAGTCTGGTCCTACGCTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTCTCTGGGTT
CTCACTCAGAACTACTGGAGAGGGTGTGGCTGGGTCCGTCAGCCCCCAGGAAAGGCCCTGGAATGGCTTGCACTCATTT
ATTGGGATGATGATAAGCGCTACAGCCCATCTCTGAAGAGCAGGCTCACCATCACCAAGGACACCTCCAAAAAGCAGGTG
GTCCTTACAATGACCAACGTGGACCCAGCGGACACAGCCACCTATTACTGTACACACGAGCAATACTATTATGATACTAG
TGGTCAGCCATACTACTTTGACTTCTGGGGCCAGGGCACCCTGGTCACCGTCTCCTCAGGCGGTGGTGGATCAGGCGCG
GAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTAACATCCAGGTGACCCAGTCTCCATCCTCCTGTCTGCATCT
GTAGGAGACAGAGTCACCATGACTTGCCGGGCGAGTCAGGACATTAGGAAGAATTTAAATTGGTATCAGCAAAAACCAGG
GAAAGCCCCTAAGGTCCTGATCTACGATGCATCCGATTTGGAAACAGGGATCCCATCAAGGTTCAGTGGAAGTCTG
GGACAGATTTTATCCTCACCATCAGCAGCCTGCAGCCTGAAGATATTGCAACATACTACTGTCAACAGTCTGATTATTTA
CCGCTCACTTTCGGCGGAGGGACCAAAGTGGATATCAAA

Amino acid sequence of a variant of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 31]:

QVTLKESGPTLVKPTQTLTLTCTFSGFSLRTTGEGVGWVRQPPGKALEWLALIYWDDDKRYSPSLKSRLTITKDTSKKQV VLTMTNVDPADTATYYCTHEQYYYDTSGQPYYFDFWGQGTLVTVSSGGGGSGGGGGGGGGGGGGGNIQVTQSPSSLSAS VGDRVTMTCRASQDIRKNLNWYQQKPGKAPKVLIYDASDLETGIPSRFSGSGSGTDFILTISSLQPEDIATYYCQQSDYL PLTFGGGTKVDIK

FIGURE 7

Amino acid sequence alignment of variants of selected scFv antibodies against loop 6 of human CCR5

V_H region:

V_L region:

15.150.11 NFMLTQPPS-ASGTPGQRVSISCSGSSS-DIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGGYPDRFSGFKSGTSASLVISGLQSEDEADYYCAAMDESINGYVFGGGTKVTVL 15.150.12 ETTLTQSPAFMSATPGDKVSISCKASR--DVDDD-VNWYQQRPGEAPIFIIEDATTLVPGISPRFSGSGGTGFTLTINNIDSEDAAYYFCLQHDNF--PLTFGGGTKVEIK 15.150.24 NIQVTQSPSSLSASVGDRVTMTCRASQ--DI-RKNLNWYQQRPGKAPKVLIYDASDLFTGIPSRFSGSGSGTDFILTISSLQPEDIATYYCQQSD-YL-PLTFGGGTKVDIK

Amino acid sequences of variable regions of clone 15.186.35 scFv against N-terminus fragment of human CCR5

V_H region [SEQ ID NO: 34]:

QVTLKESGPTLVKPTQTLTLTCTLSGFSLSTSGVSVGW1RQPPGKALEWLAS1NWNDDKCYSPSLKSRLT1TKDTPKNQV VLAMSNMDPADTATYSCALDMPPHDSGPQSFDASDVWGPGTMVTVSS

V_L region [SEQ ID NO: 35]:

3.00

SYELMQLPSVSVSPGQTASITCSGDNLGDKYACWYQQKPGRSPVLVIYGDNKRPSGIPERFSGSNSGNTATLTISGTQAM DEADYYCQAWDTSTAVFGTGTKLTVL

Partial amino acid sequences of variable regions of clone 15.150.11 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 36]:

QVQLQESGPGLVKPSETLSLTCTVSGGSIGHDYWSWIRQPPGEGLEWIGFIFFDGSTNYNPSLNGRVTISLDTSKNQLSL RLTSVTAADTAVYFCARLKGAWLLSEPPYFSSDGMDVWGQGTTVTV

V_L region [SEQ ID NO: 37]:

NFMLTQPPSAXGTPGQRVSISCSGSSSDIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGFKSGTSASLVISGLQ SEDEADYYCAAWDESLNGVVFGGG

Partial amino acid sequences of variable regions of clone 15.150.12 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 38]:

QVQLQQWGAGLLKSWGTLSLTCAVSGASFSGYYWSWIRQPPGKGLEWIGEINHRGSTTYNPSLDGRVTISLDTSTNQISL KLTSMTAADTAVYYCARTVAGTSDYWGQGTLVTVSS

V_L region [SEQ ID NO: 39]:

TTLTQSPAFMSATPGDKVSISCKASRDVDDDVNWYQQRPGEAPIFIIEDATTLVPGISPRFSGSGYGTDFTLTINNIDS EDAAYYFCLQHDNFPLTFGGGTKVEIK

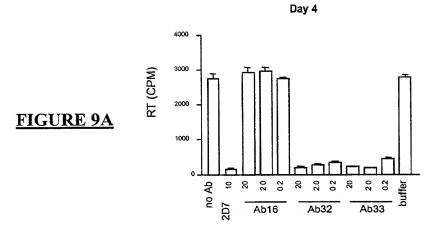
Amino acid sequences of variable regions of clone 15.150.24 scFv against loop 6 fragment of human CCR5

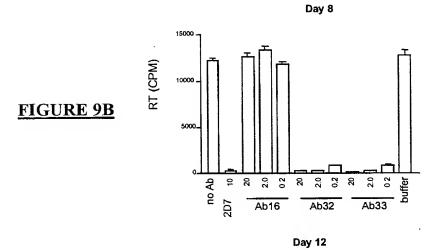
V_H region [SEQ ID NO: 40]:

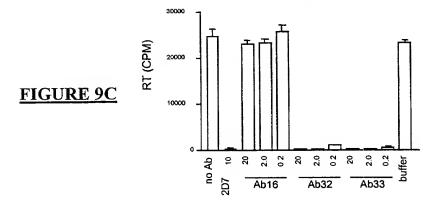
QVTLKESGPTLVKPTQTLTLTCTFSGFSLRTTGEGVGWVRQPPGKALEWLALIYWDDDKRYSPSLKSRLTITKDTSKKQV VLTMTNVDPADTATYYCTHEQYYYDTSGQPYYFDFWGQGTLVTVSS

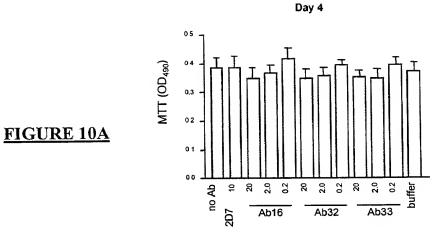
V₁ region [SEQ ID NO: 41]:

NIOVTOSPSSLSASVGDRVTMTCRASQDIRKNLNWYQQKPGKAPKVLIYDASDLETGIPSRFSGSGSGTDFILTISSLQP EDIATYYCQQSDYLPLTFGGGTKVDIK

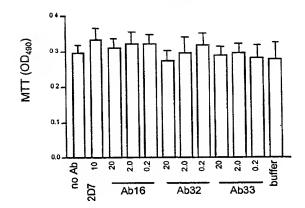












Day 8

Day 12

